

IND SAFETY REPORT: INITIAL WRITTEN REPORT

To: *Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA*
Division of Drug Oncology Products, Center for Drug Evaluation and Research, FDA

FAX: 301-796-9849

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1. IND NUMBER

7921
61010

2. AGENT NAME

Bevacizumab (rhuMab VEGF)
CCI-779 (tamsirolimus, Torisel™)

3. DATE

June 17, 2010

4. SPONSOR

Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION

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6. PHONE NUMBER

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8a. PROTOCOL NUMBER (AE #)

E2804 (AE# 1981052)

8b. AE GRADE: AE

Grade 3: Infection: Abdominal Abscess
Grade 3: Opportunistic Infection
Grade 3: Anorexia
Grade 3: Dehydration

9. PATIENT IDENTIFICATION

28244

10. AGE

63 years

11. SEX

Male

12. DESCRIPTION OF ADVERSE EVENT

The patient is 63 year-old male with renal cell adenocarcinoma who developed grade 3 abdominal abscess, grade 3 opportunistic infection, grade 3 anorexia, and grade 3 dehydration while on a phase 2 trial utilizing the investigational agents bevacizumab and CCI-779. He began the investigational therapy on January 12, 2010, and received the last dose of bevacizumab on May 4, 2010 (Cycle 5, Day 1), and the last dose of CCI-779 on May 11, 2010 (Cycle 5, Day 8). On May 14, 2010 (Cycle 5, Day 11), the patient presented to the clinic with acute abdominal pain, dehydration, anorexia, and weight loss. He was febrile with a temperature of 39.1°C. His WBC count was normal; however, he had bandemia and his C-reactive protein (CRP) was elevated at 12.6 mg/dL (reference range: 0-1 mg/dL). A CT scan of the abdomen and pelvis revealed a phlegmon and abscess between the stomach and pancreas. The patient was admitted and started on IV fluids and Zosyn®. On May 15, 2010 (Cycle 5, Day 12), the patient remained persistently febrile, so Zosyn® was changed to imipenem. On May 18, 2010 (Cycle 5, Day 15), the patient underwent aspiration of his abdominal fluid, but an attempt to place a drainage catheter was unsuccessful. A culture of abdominal fluids revealed moderate gram-negative *Staphylococcus* and presumptive *Rhizobium radiobacter*. On May 26, 2010 (Cycle 5, Day 23), the patient's condition did not improve, and his family decided to transfer him to another hospital. At the other hospital, the patient's abdominal pain improved; however, he continued to require pain medication. A VIR procedure for drainage tube insertion was recommended. At this time, the patient remains hospitalized for further evaluation. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drugs.

13. DOSE, ROUTE, AND SCHEDULE

Cycle = 28 Days.

Bevacizumab: 10 mg/kg IV over 30-90 minutes on Days 1 and 15 and CCI-779: 25 mg IV on Days 1, 8, 15, and 22

14. DATES OF TREATMENT

The patient began the investigational therapy on January 12, 2010, and received the last dose of bevacizumab on May 4, 2010 (Cycle 5, Day 1), and the last dose of CCI-779 on May 11, 2010 (Cycle 5, Day 8).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab=26,941; and CCI-779=2,068. There have been 17 other cases of opportunistic infection reported to the NCI through AdEERS as serious adverse events for bevacizumab, and 68 cases of dehydration reported to the NCI through AdEERS as serious adverse events for CCI-779. Anorexia, infection, and dehydration are expected for bevacizumab; infection, including opportunistic infections, and anorexia are expected for CCI-779.

16. COMMENTS

AT THIS TIME, NO OTHER INFORMATION IS AVAILABLE. IF UPON FURTHER INVESTIGATION RELEVANT INFORMATION BECOMES AVAILABLE, THEN A FOLLOW-UP REPORT WILL BE SUBMITTED IN ACCORDANCE WITH 21CFR 312.32(d) (2).

DISCLAIMER per 21 CFR 312.32(e): THIS SAFETY REPORT DOES NOT NECESSARILY REFLECT A CONCLUSION OR ADMISSION BY THE CTEP IDB SENIOR INVESTIGATOR/SPONSOR THAT THE INVESTIGATIONAL AGENT/THERAPY CAUSED OR CONTRIBUTED TO THE ADVERSE EXPERIENCE BEING REPORTED.